

REMARKS

Support for the above amendments can be found, for example, in the second full paragraph on page 5 teaching single chains; and in the first full paragraph on page 6 of the instant specification teaching an alkene group and radical polymerization. Hence, no issue of new matter is raised, the amendments place the application in condition for allowance, or, at the least, simplify issues for appeal, and hence, entry of the amendments is requested respectfully.

I. In item no. 3, beginning at the bottom of page 2 of the Office Action, claims 12 and 24 were rejected under 35 U.S.C. § 102(b) over U.S. Patent No. 5,143,854.

The Examiner relied on the Affymax patent teaching making microarrays and having peptides thereon made by ionic polymerization linkers in sequential, repeated reaction steps.

The rejection is traversed for the following reasons.

The '854 patent discloses a combinatorial synthesis of polypeptides that occurs in sequential reaction steps. After every step (coupling of a monomer), the monomer is light-activated to couple a further monomer. In other words, the monomers cannot transfer the activation for polymerization for the addition of the next monomer thereto without outside influence. That is not a chain reaction, which is self-perpetuating, initiated by free radical formation, but a methodical, time consuming and stepwise formation of biopolymers, limiting the '854 patent to biopolymers containing a limited number of "monomer" subunits. Moreover, the '854 method relates to constructing at the surface, the target of the assay for which the structure will be used. Finally, the target generally is a polypeptide, and the amino acid starting materials for the '854 patent are distinct from the starting materials of the instant invention.

On the other hand, current claim 24 requires in step a) a monolayer of radical polymerization initiators and the polymerization reaction occurs as a chain reaction, i.e. a reaction which is by definition continuous and does not require repeated activation steps, see page 10, fourth full paragraph of the instant application. That is, once initiated at the surface, there is a continued, self-perpetuated polymerization of the monomers to form the chains at the surface. The reactants of interest contain an alkene group suitable for such radical-induced polymerization. As opposed to the step polymerization of the '854 patent, the process of the

present invention uses a radical-propagated, and thus rapid, polymerization process which nevertheless leads to the formation of a well-ordered, functionalized polymer monolayer. This is made possible due to the concept of immobilizing radical polymerization initiators in a spatially defined manner on the surface to be modified and letting the initiators interact –after initiation of the polymerization reaction- in situ with monomers capable of taking part in and propagating the radical polymerization reaction. Also, the instant invention relates to providing a surface with enhanced reactive sites to which a completed target is bound. Hence, an end product of interest can be an intermediate having a plurality of reactive sites, however, without the target of interest bound to the polymers on the surface. An end-user can attach a target of interest to the polyfunctional polymers to provide a specific analytical device.

Accordingly, the '854 patent does not anticipate claims 24 and 12 and withdrawal of the rejection is in order.

II. In item no. 5 at the bottom of page 3 of the Office Action, claims 12 and 24 remain rejected under 35 U.S.C. § 102(e) over the Sundberg patent, U.S. Patent No. 5,919,523.

The rejection is traversed for the following reasons.

Again, as with the '854 patent discussed hereinabove, which arguments are herein incorporated by reference, the '523 patent relates to a sequential repetition of reactions requiring repeated activation, deblocking and reaction steps. That is different from the essentially, one-step chain reaction mechanism of the instant invention.

Also, the '523 patent teaches constructing the target molecule, the molecule which defines the purpose of the device, at the surface of the device. The reactants of the '523 patent is distinct from the alkene-group containing reactants of the instant invention. The result of the instant invention is an enhanced surface of reactive sites, to which a multitude of completed target molecules are bound.

Accordingly, the '523 patent does not anticipate claims 24 and 12 and withdrawal of the rejection is in order.

III. In item no. 7, beginning at the bottom of page 4 of the Office Action, claim 24 was rejected under 35 U.S.C. § 102(b) over U.S. Patent No. 5,405,746.

The rejection is traversed for the following reasons.

The '746 patent teaches a method of sequencing a nucleic acid. The nucleic acid is fixed to a surface using a functional group, such as a biotin molecule.

The '746 patent does not teach constructing a polyfunctional polymer at a surface to which a plurality of biomolecules can be bound. Also, the amplification referred to at column 4, lines 10-11 of the '746 patent relates to a primer mediated enzymatic reaction, not a radical induced polymerization reaction. Further in column 4, lines 19-25 of the '746 patent, PCR again is mentioned. However, that enzyme-mediated amplification is done separate from manufacturing the surface and is used merely to produce larger quantities of the starting target.

Hence, there is no anticipation and the rejection can be withdrawn.

IV. In item no. 8 on page 5, claim 24 was rejected under 35 U.S.C. § 102(e) over U.S. Patent No. 6,017,738.

The rejection is traversed for the following reasons.

The '738 patent teaches methods of amplifying a nucleic acid using a solid surface. A primer is attached to a surface to initiate the amplification. The primer is attached to the surface by particular chemical methods, see column 4, line 65-column 6, line 45. The amplification of the target is obtained by PCR and other amplification methods, all are enzyme-mediated amplification mechanisms, using the primer attached to the surface.

The '738 patent does not teach constructing a polyfunctional polymer at the surface using radical-mediated polymerization to yield a surface comprising multiple polymers to which a target, such as the primer of the '738 patent, is bound.

Hence, the '738 patent does not teach the claimed invention and withdrawal of the rejection is in order.

V. In item no. 10, on page 6 of the Office Action, claims 12-14 and 24 remain rejected under 35 U.S.C. § 103(a) over the Côté et al. patent, U.S. Patent No. 6,485,703, in view of the DiCosmo et al. patent, U.S. Patent No. 6,132,765.

The rejection is traversed for the following reasons.

One essential aspect of the process of the present invention is the immobilization of the polymerization initiators, so that each of the monomer chains formed in the subsequent steps is fixed at one end to a defined location (i.e. the location to which the initiator is fixed) on the surface. This approach, which allows the formation of a structurally and spatially well defined polymer monolayer, is neither taught for nor derivable by the skilled reader from the '703 patent, from the '765 patent or from both patents.

In this context, the Examiner raised a question about the fixed location of the initiators on a surface. As noted in step (a) of instant independent claim 24, the initiator is immobilized to a surface. Immobilization is taught on page 4 of the instant specification as a permanent fixation.

Such an immobilization of initiators prior to carrying out a polymerization reaction on the initiated surface is not disclosed in the passages of the '703 patent referred to in the Office Action, e.g. in column 26, line 10 thereof. The concerned paragraph of the '703 patent notes that the polymerized films are adhered to surfaces. However, the initiators prior to the polymerization reaction are merely mixed with the polymer precursors and coated onto the surface to be modified. No adherence, let alone a spatially defined one, results between the initiators and the surface before the polymerization is started in the '703 patent, and the advantages of the instant invention described above of growing polymer chains at defined locations cannot be achieved practicing the teachings of the '703 patent.

Moreover, the Examiner referred to Example 6 of Côté et al. as teaching monolayers. That example, which is well in agreement with the overall disclosure content of the '703 patent, teaches making monolayer films and layering the various films to provide a multilayered structure. However, none of the monolayers contained in the multilayer setup of the Example of the '703 patent is prepared according to the method of the present invention, starting from a monolayer of immobilized polymerization initiators and eventually resulting in a monolayer of monomer chains grown from these initiators. For example, compare that process with the

distinct process taught in the '703 patent in the section, "Polymer Synthesis" in col. 60, lines 21-62 of Example 6 which discloses the separate formation of polymers which are subsequently coated and adhered to the surface of the sensor.

In addition, it is noted that the '703 patent relates to hydrogels, which are disclosed therein in compliance with their common definition in the art as three dimensional networks of molecules that, by virtue of their crosslinked structure, are able to entrap fluids therein, hence, the name, hydrogel, see, for example, column 17, line 48; column 18, lines 64 and 65; column 21, line 10; and column 22, lines 21 and 22 which teach cross-linked, networked structures. The monomers must interconnect so as to form, for example, particles and microspheres, column 18, lines 20-21.

On the other hand, the instant invention relates to surfaces carrying polyfunctional single chain molecules.

The '765 patent teaches the formation of a polymer structure which is subsequently bound to a substrate (cf. col. 1, lines 12 to 15). The '765 patent does not disclose the immobilization of initiators to provide an initiated surface on which a polymerization reaction is carried out. As a result, the '765 patent cannot remedy the lack of disclosure of the '703 patent.

Also in terms of the polymer to be bound to the substrate, the '765 patent relates to liposomes within a hydrogel. Again, a hydrogel, such as gelatin, is a cross-linked network of molecules that defines a three-dimensional structure that can entrap liquid. The '765 patent teaches the hydrogel to be a matrix, column 4, lines 55-57, that is cross-linked, column 5, lines 60-64. The hydrogel is bound to a surface by a direction reaction scheme, paragraph bridging columns 5 and 6.

Thus, the '765 patent does not cure the deficiencies of the primary reference.

Summing up, it is noted that neither reference teaches nor suggests polyfunctional polymers which are synthesized from an initiator immobilized on a surface to form a well defined polymer monolayer on the surface. Moreover, none of the references discloses single chain polyfunctional polymers, as both references relate to hydrogels. Hydrogels are structurally different, being three dimensional networks or matrices, from the essentially linear polyfunctional polymers of interest.

Accordingly, a prime facie case of obviousness has not been made and withdrawal of the rejection is in order.

VI. In item no. 11 on page 7 of the Office Action, claims 13 and 14 were rejected under 35 U.S.C. § 103(a) over the Sundberg et al. patent in view of the Côté et al. patent.

The rejection is traversed for the following reasons.

The growing of copolymer chains from a surface on which polymerization initiators are immobilized is not suggested in either or both of the '523 and '703 patents. The irrelevance of the teachings of the two patents as to the claimed invention are provided hereinabove, which arguments are herein incorporated by reference in entirety.

Moreover, the '703 patent does not cure the deficiencies of the '523 patent.

Neither of the two references teaches or suggests the immobilization of initiators on a surface and then following initiation, enabling a continuous chain reaction of polymerization of monomers at the surface to produce the polymerized surface of interest, which polymers do not form a network such as a hydrogel of the relied on references.

Thus, a prime facie case of obviousness has not been made and withdrawal of the rejection is in order.

CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance. Reexamination, reconsideration, withdrawal of the rejections and early indication of allowance are requested respectfully. Should the Examiner believe that an interview would advance the prosecution of this application, the Examiner is invited to contact the undersigned at the exchange noted below.

Respectfully submitted,

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